that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:57:32 ON 21 JUN 2007
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 20 JUN 2007 HIGHEST RN 938114-25-1
DICTIONARY FILE UPDATES: 20 JUN 2007 HIGHEST RN 938114-25-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

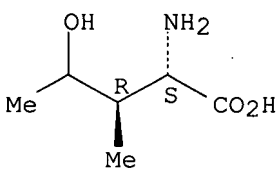
http://www.cas.org/support/stngen/stndoc/properties.html

=> s 4-hydroxyisoleucine
19583402 4
5 HYDROXYISOLEUCINE
L1 5 4-HYDROXYISOLEUCINE
(4(W)HYDROXYISOLEUCINE)

=> d 1-5

L1 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 781658-23-9 REGISTRY
ED Entered STN: 16 Nov 2004
CN L-Isoleucine, 4-hydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **4-Hydroxyisoleucine**
FS STEREOSEARCH
MF C6 H13 N O3
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS, IMSDRUGNEWS, IMSRESEARCH, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.

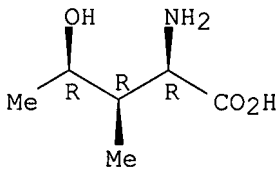


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

26 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
27 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 60010-78-8 REGISTRY
ED Entered STN: 16 Nov 1984
CN D-Xylonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(2R,3R,4R)-4-Hydroxyisoleucine**
CN (4R)-4-Hydroxy-D-alloisoleucine
FS STEREOSEARCH
DR 50764-07-3
MF C6 H13 N O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).

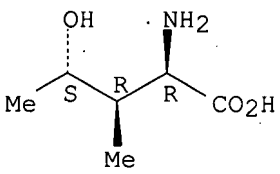


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1907 TO DATE)
9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 60010-73-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN L-Arabinonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)
OTHER NAMES:
CN **(2R,3R,4S)-4-Hydroxyisoleucine**
CN (4S)-4-Hydroxy-D-alloisoleucine
FS STEREOSEARCH
MF C6 H13 N O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).

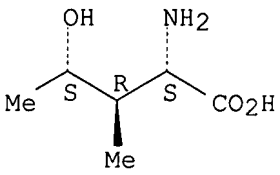


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10 REFERENCES IN FILE CA (1907 TO DATE)
10 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 55399-93-4 REGISTRY
ED Entered STN: 16 Nov 1984
CN L-Ribonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)
OTHER NAMES:
CN **(2S,3R,4S)-4-Hydroxyisoleucine**
CN (4S)-4-Hydroxy-L-isoleucine
FS STEREOSEARCH
MF C6 H13 N O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).

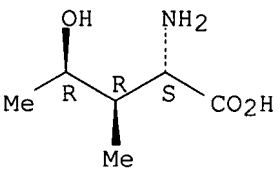


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

31 REFERENCES IN FILE CA (1907 TO DATE)
31 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 55399-92-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN D-Lyxonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Isoleucine, 4-hydroxy-, (2S,3R,4R)- (8CI)
OTHER NAMES:
CN **(2S,3R,4R)-4-Hydroxyisoleucine**
CN (4R)-4-Hydroxy-L-isoleucine
FS STEREOSEARCH
DR 21704-86-9, 50764-06-2
MF C6 H13 N O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CSCHEM, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

17 REFERENCES IN FILE CA (1907 TO DATE)
17 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus medline biosis

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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        20.10      20.31

FILE 'CAPLUS' ENTERED AT 16:58:06 ON 21 JUN 2007
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FILE 'MEDLINE' ENTERED AT 16:58:06 ON 21 JUN 2007

FILE 'BIOSIS' ENTERED AT 16:58:06 ON 21 JUN 2007
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=> s l1 or 4-hydroxyisoleucine or 4-hydroxy-L-isoleucine
L2          128 L1 OR 4-HYDROXYISOLEUCINE OR 4-HYDROXY-L-ISOLEUCINE

=> s l2 and (insulin or diabetes or insuline)
L3           59 L2 AND (INSULIN OR DIABETES OR INSULINE)

=> focus
PROCESSING COMPLETED FOR L3
L4           59 FOCUS L3 1-

=> s l4 and pd <=2000
   2 FILES SEARCHED...
L5           18 L4 AND PD <=2000

=> s l4 and (hyperinsulinemia or (high (l) insulin) or hyperinsulinism)
L6            9 L4 AND (HYPERINSULINEMIA OR (HIGH (L) INSULIN) OR HYPERINSULINI
                SM)

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7            7 DUP REM L6 (2 DUPLICATES REMOVED)

=> s l5 dup rem
MISSING OPERATOR L5 DUP
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> dup rem l5
PROCESSING COMPLETED FOR L5
L8           12 DUP REM L5 (6 DUPLICATES REMOVED)

=> d ibib abs 1-9 hitstr

L8   ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2004:999654  CAPLUS
DOCUMENT NUMBER:          141:406105
TITLE:                    Methods and compositions using β-alanylhistidine
                          peptides and β-alanines for increasing the
                          anaerobic working capacity in tissues
INVENTOR(S):              Harris, Roger; Dunnett, Mark
PATENT ASSIGNEE(S):       Natural Alternatives International, UK
SOURCE:                   U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part of U.S.
                          Ser. No. 209,169.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   4
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
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US 2004229773	A1	20041118	US 2003-717217	20031118
US 5965596	A	19991012	US 1997-909513	19970812 <--
US 6172098	B1	20010109	US 1999-318530	19990525
US 2001005579	A1	20010628	US 2001-757782	20010109
US 6426361	B2	20020730		
US 2003100513	A1	20030529	US 2002-209169	20020730
US 6680294	B2	20040120		
CA 2521987	A1	20041028	CA 2004-2521987	20040408
WO 2004091497	A2	20041028	WO 2004-US11050	20040408
WO 2004091497	A3	20050310		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1610800	A2	20060104	EP 2004-749952	20040408
JP 2006522821	T	20061005	JP 2006-509880	20040408

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.:	GB 1996-16910	A 19960812
	GB 1996-21914	A 19961021
	US 1997-909513	A3 19970812
	US 1999-318530	A1 19990525
	US 2001-757782	A1 20010109
	US 2002-209169	A2 20020730
	US 2003-462238P	P 20030410
	US 2003-717217	A 20031118
	WO 2004-US11050	W 20040408

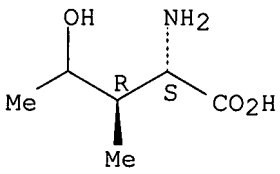
AB The invention provides compns. comprising β-alanylhistidine peptides and β-alanines, and methods for administering these peptides and amino acids. In one aspect, the compns. and methods cause an increase in the blood plasma concns. of βeta-alanine and/or creatine.

IT **781658-23-9**
RL: BUU (Biological use, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-alanylhistidine peptides and β-alanines for increasing anaerobic working capacity in tissues)

RN 781658-23-9 CAPLUS

CN L-Isoleucine, 4-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1

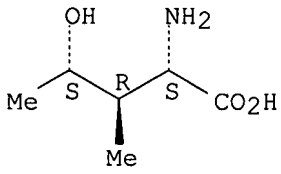
ACCESSION NUMBER: 2000:156040 CAPLUS

DOCUMENT NUMBER: 132:317627

TITLE: **4-Hydroxyisoleucine**: effects of synthetic and natural analogues on **insulin** secretion

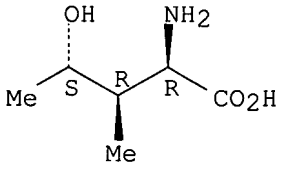
AUTHOR(S): Broca, C.; Manteghetti, M.; Gross, R.; Baissac, Y.; Jacob, M.; Petit, P.; Sauvaire, Y.; Ribes, G.
CORPORATE SOURCE: UMR 9921 du Centre National de la Recherche Scientifique, Montpellier, Fr.
SOURCE: European Journal of Pharmacology (**2000**), 390(3), 339-345
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **4-Hydroxyisoleucine**, a peculiar amino acid extracted from fenugreek seeds and never found in mammalian tissues, exhibits interesting insulinotropic activity. To investigate the structural requirements for this stimulating effect, the insulinotropic activity of the major isomer (2S,3R,4S) of **4-hydroxyisoleucine**, in the presence of 8.3 mM glucose, was compared to that of its minor isomer (2R,3R,4S), its lactone form, classical structurally related amino acids, and synthetic monomethylated analogs. In the isolated, ex vivo, perfused rat pancreas, only the major isomer of **4-hydroxyisoleucine** (200 μM) potentiated **insulin** release. On incubated isolated rat islets, the threshold concentration for a significant increase ($P<0.05$) in **insulin** release was 200 μM for (2S,3R,4S) **4-hydroxyisoleucine**, 500 μM for (2S,4R) and (2S,4S) γ-hydroxynorvalines as well as (2S,3S) and (2S,3R) γ-hydroxyvalines, and 1 mM or more for other congeners. In conclusion, the insulinotropic properties of **4-hydroxyisoleucine**, in the micromolar range, are seen only in the presence of the linear major isoform; they also require carbon α in S-configuration, full methylation and carbon γ-hydroxylation.
IT **55399-93-4**, (2S,3R,4S)-**4-Hydroxyisoleucine**
60010-73-3, (2R,3R,4S)-**4-Hydroxyisoleucine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structural requirements for insulinotropic effect of **4-Hydroxyisoleucine** in isolated rat pancreas)
RN 55399-93-4 CAPLUS
CN L-Ribonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 60010-73-3 CAPLUS
CN L-Arabinonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 1999:714049 CAPLUS
DOCUMENT NUMBER: 132:44784
TITLE: **4-Hydroxyisoleucine**: experimental evidence of its insulinotropic and antidiabetic properties
AUTHOR(S): Broca, Christophe; Gross, Rene; Petit, Pierre; Sauvaire, Yves; Manteghetti, Michele; Tournier, Michel; Masiello, Pellegrino; Gomis, Ramon; Ribes, Gerard
CORPORATE SOURCE: Unite Mixte de Recherche 9921 du Centre National de la Recherche Scientifique, and Faculte de Medecine and Laboratoire de Recherche sur les Substances Naturelles Vegetales, UPRES EA 1677, Laboratoire de Pharmacologie, Montpellier, 34060, Fr.
SOURCE: American Journal of Physiology (**1999**), 277(4, Pt. 1), E617-E623
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have recently shown in vitro that **4-hydroxyisoleucine** (4-OH-Ile), an amino acid extracted from fenugreek seeds, potentiates **insulin** secretion in a glucose-dependent manner. The present study was designed to investigate whether 4-OH-Ile could exert in vivo insulinotropic and antidiabetic properties. For this purpose, i.v. or oral glucose tolerance tests (IVGTTs and OGTTs, resp.) were performed not only in normal animals but also in a type II **diabetes** rat model. During IVGTT in normal rats or OGTT in normal dogs, 4-OH-Ile (18 mg/kg) improved glucose tolerance. The lactonic form of 4-OH-Ile was ineffective in normal rats. In non-**insulin**-dependent diabetic (NIDD) rats, a single i.v. administration of 4-OH-Ile (50 mg/kg) partially restored glucose-induced **insulin** response without affecting glucose tolerance; a 6-day subchronic administration of 4-OH-Ile (50 mg/kg, daily) reduced basal hyperglycemia, decreased basal insulinemia, and slightly, but significantly, improved glucose tolerance. In vitro, 4-OH-Ile (200 μM) potentiated glucose (16.7 mM)-induced **insulin** release from NIDD rat-isolated islets. So, the antidiabetic effects of 4-OH-Ile on NIDD rats result, at least in part, from a direct pancreatic B cell stimulation.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:507230 CAPLUS
DOCUMENT NUMBER: 129:269766
TITLE: Antidiabetic and hypocholesterolemic effects of fenugreek
AUTHOR(S): Al-Habbori, Molham; Raman, Amala
CORPORATE SOURCE: Department of Clinical Biochemistry, Faculty of Medicine and Health Sciences, University of Sana'a, Sana'a, Yemen
SOURCE: Phytotherapy Research (**1998**), 12(4), 233-242
CODEN: PHYREH; ISSN: 0951-418X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with many refs. The seeds of Trigonella foenum graecum (fenugreek) have been reported to have antidiabetic and hypocholesterolemic properties in both animal models and humans. Activity has been attributed largely to fenugreek's saponin and high fiber content, and is probably not related to its major alkaloid trigonelline. Antihyperglycemic effects have been linked to delayed gastric emptying caused by the fiber content, and to (unidentified) components that inhibit

carbohydrate digestive enzymes. Fenugreek administration may increase plasma **insulin** levels in vivo. Its major free amino acid, **4-hydroxyisoleucine**, stimulates **insulin** secretion from perfused pancreas in vitro. The hypocholesterolemic effect has been attributed to increased conversion of hepatic cholesterol to bile salts due to loss, in the feces, of complexes of these substances with fenugreek fiber and saponins. Fenugreek treatment selectively reduces the LDL and VLDL fractions of total cholesterol, and HDL-cholesterol has also been reported to increase in alloxan-induced diabetic rats and type II diabetic individuals following treatment with fenugreek. Fenugreek administration has not been reported to cause any toxicol. effects. Its regular consumption may therefore be beneficial in the management of **diabetes** and the prevention of atherosclerosis and coronary heart disease.

REFERENCE COUNT: 129 THERE ARE 129 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 1998:70710 CAPLUS
DOCUMENT NUMBER: 128:200858
TITLE: **4-Hydroxyisoleucine**: a novel amino acid potentiator of **insulin** secretion
AUTHOR(S): Sauvaire, Yves; Petit, Pierre; Broca, Christophe; Manteghetti, Michele; Baissac, Yves; Fernandez-Alvarez, Josepha; Gross, Rene; Roye, Michele; Leconte, Agnes; Gomis, Ramon; Ribes, Gerard
CORPORATE SOURCE: Laboratoire de Recherche sur les Substances Naturelles Vegetales, Unite Propre de Recherche Enseignement Superieur EA 1677, Universite Montpellier II, Montpellier, 34095, Fr.
SOURCE: Diabetes (**1998**), 47(2), 206-210
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors report the characterization of a new insulinotropic compound, **4-hydroxyisoleucine**. This amino acid has been extracted and purified from fenugreek seeds, which are known in traditional medicine for their antidiabetic properties. **4-Hydroxyisoleucine** increases glucose-induced **insulin** release, in the concentration range of 100 μM to 1 mM, through a direct effect on isolated islets of Langerhans from both rats and humans. The stimulating effect of **4-hydroxyisoleucine** was strictly glucose dependent; indeed, ineffective at low (3 mM) or basal (5 mM) glucose concns., the amino acid potentiated the **insulin** secretion induced by supranormal (6.6-16.7 mM) concns. of glucose. In addition, in the isolated perfused rat pancreas, the authors could show (1) that the pattern of **insulin** secretion induced by **4-hydroxyisoleucine** was biphasic, (2) that this effect occurred in the absence of any change in pancreatic α- and δ-cell activity, and (3) that the more glucose concentration was increased, the more **insulin** response was amplified. Moreover, **4-hydroxyisoleucine** did not interact with other agonists of **insulin** secretion (leucine, arginine, tolbutamide, glyceraldehyde). Therefore, the authors conclude that **4-hydroxyisoleucine** insulinotropic activity might, at least in part, account for fenugreek seeds' antidiabetic properties. This secretagogue may be considered as a novel drug with potential interest for the treatment of NIDDM.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:617969 CAPLUS

DOCUMENT NUMBER: 127:257635
TITLE: Antidiabetic composition containing (2S, 3R, 4S)-**4-hydroxyisoleucine**
INVENTOR(S): Sauvaire, Yves; Ribes, Gerard
PATENT ASSIGNEE(S): Societe Civile de Gestion Jouvenet, Fr.; Sauvaire, Yves; Ribes, Gerard
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732577	A1	19970912	WO 1997-FR420	19970307 <--
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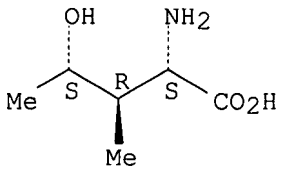
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2745718	A1	19970912	FR 1996-2955	19960308 <--
FR 2745718	B1	19980507		
AU 9720319	A	19970922	AU 1997-20319	19970307 <--

PRIORITY APPLN. INFO.: FR 1996-2955 A 19960308
WO 1997-FR420 W 19970307

AB An antidiabetic composition capable of stimulating **insulin** secretion and particularly suitable for treating non-**insulin**-dependent **diabetes** is disclosed. The composition contains (2S, 3R, 4S)-**4-hydroxyisoleucine**, and/or the lactone form thereof, and is substantially free of any other stereoisomer of this compound

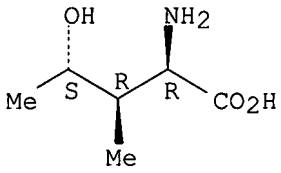
IT **55399-93-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hydroxyisoleucine isomer antidiabetic composition)
RN 55399-93-4 CAPLUS
CN L-Ribonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **60010-73-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(hydroxyisoleucine isomer antidiabetic composition)
RN 60010-73-3 CAPLUS
CN L-Arabinonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



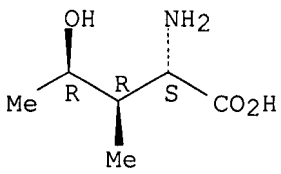
L8 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1997:116899 CAPLUS
DOCUMENT NUMBER: 126:247872
TITLE: Characterization of a dioxygenase from Trigonella foenum-graecum involved in **4-hydroxyisoleucine** biosynthesis
AUTHOR(S): Haefele, Catherine; Bonfils, Claude; Sauvaire, Yves
CORPORATE SOURCE: Lab. Rech. Substances Naturelles Vegetales, Univ. Montpellier II, Montpellier, 30495, Fr.
SOURCE: Phytochemistry (**1997**), 44(4), 563-566
CODEN: PYTCAS; ISSN: 0031-9422
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **4-Hydroxyisoleucine**, an unusual amino acid known for its **insulin**-stimulating effect, was detected by HPLC following isoleucine incubation with a cell-free extract from etiolated 6-day-old fenugreek seedlings in the presence of various cofactors. The reaction showed that **4-hydroxyisoleucine** formation is dependent on the presence of Fe2+, 2-oxoglutarate, ascorbate and oxygen. This suggests that a 2-oxoacid-dependent dioxygenase plays a key role in this biosynthetic pathway.

IT **55399-92-3**
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(formation of **insulin**-stimulating amino acid by fenugreek cell-free extract)

RN 55399-92-3 CAPLUS
CN D-Lyxonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 8 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:370719 BIOSIS
DOCUMENT NUMBER: PREV199799669922
TITLE: Calcium signalling is involved in the **insulin**-releasing effect of **4-hydroxyisoleucine**
AUTHOR(S): Petit, P. [Reprint author]; Liu, Y. J.; Broca, C. [Reprint author]; Sauvaire, Y.; Ribes, G. [Reprint author]; Gylfe, E.
CORPORATE SOURCE: Lab. Pharmacol., Fac. Med., Univ. Montpellier, II Montpellier, France
SOURCE: Diabetologia, (**1997**) Vol. 40, No. SUPPL. 1, pp. A112.
Meeting Info.: 16th International Diabetes Federation

Congress. Helsinki, Finland. July 20-25, 1997.
CODEN: DBTGAJ. ISSN: 0012-186X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Sep 1997
Last Updated on STN: 4 Sep 1997

L8 ANSWER 9 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:452132 BIOSIS
DOCUMENT NUMBER: PREV199699174488
TITLE: Could **4-hydroxyisoleucine** be used as a hypoglycaemic agent in the treatment of type 2 **diabetes** mellitus?.
AUTHOR(S): Fernandez-Alvarez, J. [Reprint author]; Sauvaire, Y.; Petit, P.; Casamitjana, R.; Ribes, G.; Gomis, R.
CORPORATE SOURCE: Endocrinol. Unit/Hormonal Lab., Hosp. Clinic, Barcelona, Spain
SOURCE: Diabetologia, (**1996**) Vol. 39, No. SUPPL. 1, pp. A234.
Meeting Info.: 32nd Annual Meeting of the European Association for the Study of Diabetes. Vienna, Austria. September 1-5, 1996.
CODEN: DBTGAJ. ISSN: 0012-186X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Oct 1996
Last Updated on STN: 7 Oct 1996

=> d ibib abs hitstr 10-12

L8 ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:452133 BIOSIS
DOCUMENT NUMBER: PREV199699174489
TITLE: Structure activity analysis of different analogues of the new insulinotropic agent **4-hydroxyisoleucine**.
AUTHOR(S): Ribes, G. [Reprint author]; Broca, C.; Petit, P.; Jacob, M.; Baissac, Y.; Manteghetti, M.; Roye, M.; Sauvaire, Y.
CORPORATE SOURCE: Fac. Med., UMR 9921 CNRS, Univ. Montpellier II, France
SOURCE: Diabetologia, (**1996**) Vol. 39, No. SUPPL. 1, pp. A234.
Meeting Info.: 32nd Annual Meeting of the European Association for the Study of Diabetes. Vienna, Austria. September 1-5, 1996.
CODEN: DBTGAJ. ISSN: 0012-186X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Oct 1996
Last Updated on STN: 7 Oct 1996

L8 ANSWER 11 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:425001 BIOSIS
DOCUMENT NUMBER: PREV199598439301
TITLE: **Insulin** stimulating effect of an original amino acid, **4-hydroxyisoleucine**, purified

from fenugreek seeds.
AUTHOR(S): Petit, P.; Sauvaire, Y.; Hillaire-Buys, D.; Manteghetti, M.; Baissac, Y.; Gross, R.; Ribes, G.
CORPORATE SOURCE: Lab. Pharmacol., Fac. Med., UMR 9921 CNRS, Lab. Recherche Substances Naturelles Vegetales, Montpellier, France
SOURCE: Diabetologia, (**1995**) Vol. 38, No. SUPPL. 1, pp. A101.
Meeting Info.: 31st Annual Meeting of the European Association for the Study of Diabetes. Stockholm, Sweden. September 12-16, 1995.
CODEN: DBTGAJ. ISSN: 0012-186X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Oct 1995
Last Updated on STN: 3 Oct 1995

L8 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:280270 CAPLUS
DOCUMENT NUMBER: 120:280270
TITLE: Pharmaceutical compositions containing mono or polyhydroxylated amino acids for the treatment of non-**insulin** dependent **diabetes** mellitus
INVENTOR(S): Sauvaire, Yves; Ribes, Gerard
PATENT ASSIGNEE(S): Laboratoires Monal, Fr.
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 587476	A1	19940316	EP 1993-402135	19930901 <--
EP 587476	B1	19980318		
R: AT, BE, CH, DE, DK, ES, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2695317	A1	19940311	FR 1992-10644 .	19920907 <--
FR 2695317	B1	19950310		
JP 06157302	A	19940603	JP 1993-217588	19930901 <--
AT 164064	T	19980415	AT 1993-402135	19930901 <--
ES 2116421	T3	19980716	ES 1993-402135	19930901 <--
CA 2105502	A1	19940308	CA 1993-2105502	19930903 <--
CA 2105502	C	20001121		
IN 183194	A1	19991002	IN 1994-DE244	19940301 <--

PRIORITY APPLN. INFO.: FR 1992-10644 A 19920907
AB The title amino acids are extracted from plants and are used as antidiabetic agents. Thus, **4-hydroxyisoleucine** was extracted from fenugreek seeds (preparation given) and used at 500μM on isolated rat pancreas in presence of 8.3mM glucose for 10min. The amount of **insulin** secreted was 2206 as compared to 810μM.

=> d ibib abs hitstr 1-7 17

L7 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2005:146900 CAPLUS
DOCUMENT NUMBER: 142:410368
TITLE: The addition of fenugreek extract (Trigonella foenum-graecum) to glucose feeding increases muscle glycogen resynthesis after exercise
AUTHOR(S): Ruby, B. C.; Gaskill, S. E.; Slivka, D.; Harger, S. G.
CORPORATE SOURCE: Department of Health and Human Performance, The

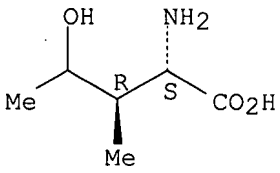
University of Montana, Missoula, MT, USA
SOURCE: Amino Acids (2005), 28(1), 71-76
CODEN: AACIE6; ISSN: 0939-4451
PUBLISHER: Springer Wien
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to determine the effects of ingesting an oral supplement containing **4-Hydroxyisoleucine** (4-OH-Ile, isolated from fenugreek seeds [Trigonella foenum-graecum]) with a glucose beverage on rates of post-exercise muscle glycogen resynthesis in trained male cyclists. Following an overnight fast (12 h), subjects completed a 90-min glycogen depletion ride after which a muscle biopsy was obtained from the vastus lateralis. Immediately and 2 h after the muscle biopsy, subjects ingested either an oral dose of dextrose (Glu) (1.8 g·kg BW-1) or 4-OH-Ile supplement (Glu + 4-OH-Ile, including 2.0 mg·kg-1 4-OH-Ile with the same oral dose of dextrose) with a second muscle biopsy 4 h after exercise. Post exercise muscle glycogen concentration was similar for both trials. Overall, there was a significant increase in glucose and **insulin** concns. from time 0 throughout the majority of the 4-h recovery period, with no significant differences between the two trials at any time point. Although muscle glycogen concentration significantly increased from immediately post exercise to 4 h of recovery for both trials, the net rate of muscle glycogen resynthesis was 63 greater during Glu + 4-OH-Ile (10.6±3.3 vs. 6.5±2.6 g·kg wet weight-1·hr.-1 for the Glu + 4-OH-Ile and Glu trials, resp.). These data demonstrate that when the fenugreek extract supplement (4-OH-Ile) is added to a **high** oral dose of dextrose, rates of post-exercise glycogen resynthesis are enhanced above dextrose alone.

IT **781658-23-9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(the addition of fenugreek extract (Trigonella foenum-graecum) to glucose feeding increases muscle glycogen resynthesis after exercise)

RN 781658-23-9 CAPLUS
CN L-Isoleucine, 4-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 7 MEDLINE on STN
ACCESSION NUMBER: 2004404025 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15082420
TITLE: Insulinotropic agent ID-1101 (**4-hydroxyisoleucine**) activates **insulin** signaling in rat.
AUTHOR: Broca Christophe; Breil Vincent; Cruciani-Guglielmacci Celine; Manteghetti Michele; Rouault Christine; Derouet Michel; Rizkalla Salwa; Pau Bernard; Petit Pierre; Ribes Gerard; Ktorza Alain; Gross Rene; Reach Gerard; Taouis Mohammed
CORPORATE SOURCE: Laboratoire de Pharmacologie, Centre de Pharmacologie et Biotechnologies pour la Sante-Unite Mixte de Recherche 5160 Centre National de la Recherche Scientifique, Faculte de Medecine, 34060 Montpellier, France.. christophe.broca@univ-

montp1.fr
SOURCE: American journal of physiology. Endocrinology and metabolism, (2004 Sep) Vol. 287, No. 3, pp. E463-71. Electronic Publication: 2004-04-13. Journal code: 100901226. ISSN: 0193-1849.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 14 Aug 2004
Last Updated on STN: 11 Sep 2004
Entered Medline: 10 Sep 2004

AB ID-1101 (**4-hydroxyisoleucine**), an amino acid extracted from fenugreek seeds, exhibits an interesting glucose-dependent **insulin**-stimulating activity. The present study was undertaken to investigate a possible extrapancreatic effect of ID-1101 on **insulin** signaling and action besides its previously described insulinotropic action. **Insulin**-sensitizing effects of ID-1101 were investigated in rat in vivo by three different approaches: 1) using euglycemic hyperinsulinemic clamps in two different rat models of **insulin** resistance, i.e., Zucker fa/fa rats and rats fed a sucrose-lipid diet; 2) measuring liver and muscle phosphatidylinositol (PI) 3-kinase activity after an acute injection of ID-1101 in normal and **insulin**-resistant diabetic rats; and 3) after chronic treatment in two rat models of **insulin** resistance. Euglycemic hyperinsulinemic clamp experiments revealed that ID-1101 can improve **insulin** resistance through an increase of peripheral glucose utilization rate in sucrose-lipid-fed rats and by decreasing hepatic glucose production in Zucker fa/fa rats. Moreover, we demonstrated that a single injection of ID-1101 activates the PI 3-kinase activity in liver and muscle from normal rats but also in muscle from diabetic rats. Finally, chronic ID-1101 treatment significantly reduced insulinemia in type 2 diabetic rats and reduced the progression of **hyperinsulinemia** in **insulin**-resistant obese Zucker fa/fa rats. These findings clearly demonstrate that ID-1101 can reduce **insulin** resistance through activation of the early steps of **insulin** signaling in peripheral tissues and in liver. In summary, ID-1101, besides its insulinotropic effect, directly improves **insulin** sensitivity, making it a potentially very valuable therapeutic agent for **diabetes** treatment.

L7 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:435594 CAPLUS
TITLE: Exploring Synthetic Routes to 4-Hydroxyamino Acids: Potential Blood Glucose Regulating Agents
AUTHOR(S): Davies, Don R.; Vellinga, Jonathan
CORPORATE SOURCE: Chemistry, Weber State University, Ogden, UT, 84408, USA
SOURCE: Abstracts, Joint Regional Meeting of the Northwest and Rocky Mountain Sections of the American Chemical Society, Logan, UT, United States, June 6-9 (2004), GEN-140. American Chemical Society: Washington, D. C. CODEN: 69FLZI
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB **4-Hydroxyisoleucine**, a rare amino acid found only in few plant sources, has been found to possess potent **insulin** releasing activity in the presence of moderate to **high** blood glucose concns., and therefore, may be used in the treatment of hyperglycemia. Since **4-hydroxyisoleucine** is difficult to isolate from plant sources we wish to synthetically produce it on a larger scale in our labs. Addnl., a synthetic approach provides

flexibility to producing other 4-hydroxyamino acids that may have improved properties over **4-hydroxyisoleucine**. In our presentation we will discuss and compare possible synthetic routes leading to 4-hydroxyamino acids. We will also address what we have accomplished toward the synthesis of these rare aminoacids and what we hope to accomplish in the near future.

L7 ANSWER 4 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:13813 BIOSIS
DOCUMENT NUMBER: PREV200400013001
TITLE: The insulinotropic agent **4-hydroxyisoleucine** also activates **insulin** signaling in vivo and in vitro.
AUTHOR(S): Broca, C. [Reprint Author]; Breil, V.; Manteghetti, M. [Reprint Author]; Derouet, M.; Petit, P. [Reprint Author]; Ribes, G. [Reprint Author]; Gross, R. [Reprint Author]; Reach, G.; Taouis, M.
CORPORATE SOURCE: Laboratoire de Pharmacologie du Diabete, CNRS UMR 5094, Montpellier, France
SOURCE: Diabetes & Metabolism, (August 2003) Vol. 29, No. Hors serie 2, pp. 4S96. print.
Meeting Info.: 18th International Diabetes Federation Congress. Paris, France. August 24-29, 2003.
ISSN: 1262-3636.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Dec 2003
Last Updated on STN: 24 Dec 2003

L7 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:167800 CAPLUS
DOCUMENT NUMBER: 134:202704
TITLE: Use of amino acids for making medicines for treating **insulin**-resistance
INVENTOR(S): Ribes, Gerard; Taouis, Mohammed; Petit, Pierre Roger; Broca, Christophe; Sauvaire, Yves; Pau, Bernard
PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique (CNRS), Fr.; Institut National de la Recherche Agronomique (INRA)
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015689	A1	20010308	WO 2000-FR2361	20000823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2797767	A1	20010302	FR 1999-10874	19990827
FR 2797767	B1	20020614		
CA 2382835	A1	20010308	CA 2000-2382835	20000823
EP 1206257	A1	20020522	EP 2000-958726	20000823

EP 1206257	B1	20041103			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
JP 2003508435	T	20030304	JP 2001-519903		20000823
EP 1421937	A1	20040526	EP 2003-291523		20000823
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY					
AT 281159	T	20041115	AT 2000-958726		20000823
PT 1206257	T	20050331	PT 2000-958726		20000823
ES 2231247	T3	20050516	ES 2000-958726		20000823
ZA 2002001619	A	20030526	ZA 2002-1619		20020226
HK 1052456	A1	20051028	HK 2002-108489		20021122
PRIORITY APPLN. INFO.:			FR 1999-10874	A	19990827
			EP 2000-958726	A3	20000823
			WO 2000-FR2361	W	20000823

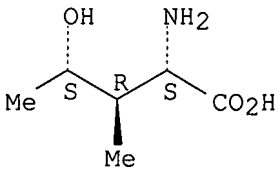
AB The invention concerns the use of monohydroxy or polyhydroxy amino acids, and the lactone forms thereof for making medicines with **insulin** -analog and/or **insulin**-sensitizing effects on peripheral tissues targeted by **insulin**, and more particularly the use thereof for making medicines for treating and preventing **insulin**-resistance. Injection of 200 μg/kg 4-hydroxy isoleucine i.p. induced the activation of **insulin** receptor and **insulin** receptor substrate-1 which was comparable to **insulin** injection.

IT **55399-93-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of amino acids for making medicines for treating **insulin** -resistance)

RN 55399-93-4 CAPLUS

CN L-Ribonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 6 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:594815 BIOSIS

DOCUMENT NUMBER: PREV200200594815

TITLE: Effect of **4-hydroxyisoleucine** on **insulin** sensitivity in **insulin** resistant rats.

AUTHOR(S): Breil, V. [Reprint author]; Rouault, C. [Reprint author]; Rizkalla, S. [Reprint author]; Broca, C.; Taouis, M.; Petit, P.; Reach, G. [Reprint author]

CORPORATE SOURCE: Service de Diabetologie, INSERM U341, Hotel-Dieu, Paris, France

SOURCE: Diabetologia, (August, 2001) Vol. 44, No. Supplement 1, pp. A 79. print.
Meeting Info.: 37th Annual Meeting of the European Association for the Study of Diabetes. Glasgow, Scotland, UK. September 09-13, 2001. European Association for the Study of Diabetes.
CODEN: DBTGAJ. ISSN: 0012-186X.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 20 Nov 2002
Last Updated on STN: 20 Nov 2002

L7 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:507230 CAPLUS
DOCUMENT NUMBER: 129:269766
TITLE: Antidiabetic and hypocholesterolemic effects of fenugreek
AUTHOR(S): Al-Habbori, Molham; Raman, Amala
CORPORATE SOURCE: Department of Clinical Biochemistry, Faculty of Medicine and Health Sciences, University of Sana'a, Sana'a, Yemen
SOURCE: Phytotherapy Research (1998), 12(4), 233-242
CODEN: PHYREH; ISSN: 0951-418X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with many refs. The seeds of Trigonella foenum graecum (fenugreek) have been reported to have antidiabetic and hypocholesterolemic properties in both animal models and humans. Activity has been attributed largely to fenugreek's saponin and **high** fiber content, and is probably not related to its major alkaloid trigonelline. Antihyperglycemic effects have been linked to delayed gastric emptying caused by the fiber content, and to (unidentified) components that inhibit carbohydrate digestive enzymes. Fenugreek administration may increase plasma **insulin** levels in vivo. Its major free amino acid, **4-hydroxyisoleucine**, stimulates **insulin** secretion from perfused pancreas in vitro. The hypocholesterolemic effect has been attributed to increased conversion of hepatic cholesterol to bile salts due to loss, in the feces, of complexes of these substances with fenugreek fiber and saponins. Fenugreek treatment selectively reduces the LDL and VLDL fractions of total cholesterol, and HDL-cholesterol has also been reported to increase in alloxan-induced diabetic rats and type II diabetic individuals following treatment with fenugreek. Fenugreek administration has not been reported to cause any toxicol. effects. Its regular consumption may therefore be beneficial in the management of **diabetes** and the prevention of atherosclerosis and coronary heart disease.

REFERENCE COUNT: 129 THERE ARE 129 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT